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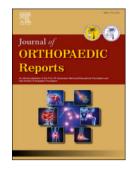
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# **Credit author statement:**

A.M. is responsible for conceptualization, researching, writing the primary draft, and editing the final manuscript.

Title page:

# Risk Factors of Vitamin D Deficiency Following Corrective Spinal Surgery in Adolescent Idiopathic Scoliosis: a narrative review

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### Risk Factors of Vitamin D Deficiency Following Corrective Spinal Surgery in Adolescent Idiopathic Scoliosis: a narrative review

#### Abstract:

Adolescent idiopathic scoliosis (AIS) is a common rigid structural spinal deformity with unknown etiology. It has been associated with low bone mineral density and osteopenia. Vitamin D has an essential role in bone health and mineralization. So it is assumed that vitamin D deficiency (VDD) is associated with the onset and development of AIS. Risk factors of VDD in general population had been introduced and discussed widely but those involved in patients after corrective spinal surgery are debated. Here we review the most dominant risk factors associated with VDD in AIS patients following corrective spinal surgery. Preoperative VDD is probably the main risk factor of postoperative VDD. Female gender, eating disorders, dressing habits, physical inactivity, and increased bone turnover are the most important contributors of preoperative VDD. ICU admission, pain, medications, surgical complications, delirium, stress response, and bracing are probably the main risk factors of VDD postoperatively. The risk factor modifications and nutritional supplementation could profoundly impact surgical outcomes in this high-risk group of patients.

Introduction:

Adolescent idiopathic scoliosis (AIS) is a common orthopedic disorder with persistent structural rotational curvature of the spine. The etiology of AIS is largely unknown but genetic, metabolic, neuromuscular, and environmental causes have been proposed. It has been demonstrated that AIS is associated with low bone mineral density and osteopenia.[1]

Vitamin D has an essential role in maintaining a healthy mineralized skeleton through promoting intestinal calcium absorption, balancing calcium– phosphate equilibrium, and regulating osteoblasts proliferation and survival. Vitamin D is acquired through cutaneous production and dietary sources and supplements. However, vitamin D deficiency (VDD) is a common health concern in general population.

It is assumed that VDD is associated with the onset and development of AIS.[2] The prevalence of VDD is higher in AIS patients compared with the general population.[2] It has been reported that VDD is associated with curve progression in these patients. Supplementation with vitamin D and calcium had been associated with controlling the progression of curvature.[3] For patients who require corrective spinal surgery, preoperative VDD has been associated with poor postoperative outcomes.[4]

Risk factors of VDD in general population had been discussed widely. Poor nutrition, reduced exposure to sunlight, low physical activity, and some medications are the most common causes of VDD in general population. However, the risk factors of VDD among AIS patients are probably different from general population. These patients are adolescents at their puberty with increased need of vitamin D and other supplements. Majority of patients are girls with irregular menstrual cycles and increased psychological discomforts. Inappropriate dietary habits and sunlight avoidance are also common in this age group. Bracing and decreased physical activity could potentially result in VDD. On the other hand, corrective spinal surgery induces a major physical and psychological stress to AIS patients perioperatively. This could exacerbate VDD status in AIS patients if not accordingly addressed perioperatively. Previous studies have focused on VDD risk factors among AIS patients preoperatively. Here we review the proposed postoperative risk factors of VDD in patients undergone corrective spinal surgery. We believe that the risk factor modifications and nutritional supplementation could profoundly impact surgical outcomes in this high-risk group of patients.

# Preoperative VDD:

Vitamin D insufficiency and deficiency are common among AIS patients scheduled for corrective spinal surgery.[5, 6] Preoperative VDD is probably the most important risk factor of postoperative VDD in AIS patients.

VDD is more common among girls with AIS. They usually follow culture of overdieting and unhealthy weight loss and have more inappropriate dietary habits. Depression and other mood disorders are also prevalent among adolescent girls. Girls are usually less sun-exposed and physically active compared to their peer boys. The use of sunscreen or sun avoidance is a common fashion among adolescent girls.

adolescents with AIS experience different aspects of Additionally, psychological discomfort in the forms of anxiety, stress, distortion of the body image, reduced self-esteem, negative emotions, and communication problems.[7] These psychological discomforts could potentially cause eating avoidance, problems. outdoor physical inactivity, and treatment uncooperativeness including the mineral supplement discontinuation. This may lead to nutritional VDD preoperatively. Drugs used for these psychological discomforts including mood stabilizers may potentially exacerbate VDD.

Bone turnover is also increased in patients with AIS.[8] Establishment of normal bone in these patients needs additional vitamin D and calcium, so depleting vitamin D reservoir in tissues, worsening VDD status. Vitamin D receptor polymorphism had also been proposed as a risk factors of VDD in AIS patients.[9]

## ICU admission:

ICU admission is usually required after corrective spinal surgery mostly due to complex surgical procedure, high level of blood loss, and prolonged operation time. The mean duration of ICU stay is about 1.9-3.0 days and could be longer in combined anteroposterior procedures and additional comorbidities.[10]

During this period, mechanical ventilation, hemodynamic instability, acidosis, hypercapnia, and hypoxemia may occur with major influences on vitamin D and calcium levels. Actually, rapid falls in circulating vitamin D levels have

been reported in patients after ICU admission. Although the exact mechanism is unknown, hepatic dysfunction, renal wasting, disrupted metabolism, fluid resuscitation, interstitial extravasation, and increased tissue conversion are probably involved.[11]

Postoperative ileus is a common concern in patients admitted to ICU after corrective spinal surgery. The prevalence of postoperative ileus is about 13.6% and surgery in the lumbar spine or major spine surgery involving more than 3 levels were reported as its risk factors.[12, 13] Surgical stress, secretion of inflammatory mediators, opioids use, alterations in hormone levels, and electrolytes and fluids imbalances have been reported as its probable etiologies. Ileus could delay dietary intake of vitamin D and interfere with its intestinal absorption. Superior mesenteric artery syndrome is a rare complication of scoliosis surgery with the same symptoms.

ICU admission has been associated with postoperative delirium and cognitive dysfunction. The prevalence of postoperative cognitive dysfunction in AIS patients is about 28.8% within seven days of the surgery.[14] Postoperative cognitive dysfunction could interfere with physical independence and ambulation, negatively affecting surgical outcomes. It could also prolong ICU stay and hospitalization. Cognitive dysfunction could impair nutritional recovery postoperatively leading to nutritional VDD.

Sleep quality of AIS patients is poor and hospitalization and ICU admission may deteriorate the condition.[15] Poor sleep quality could last up to 6 months postoperatively.[16] Changes in environment, noises, unavailability of familial support, and medications could be the etiologies of poor sleep quality in ICU patients.[17] Sleep disturbance and excessive daytime sleepiness may cause in appetite, eating disorders, and emotional distress leading to malnutrition and VDD. On the other hand, increased hospital stay is associated with physical inactivity and poor nutritional status. Immobility and bed rest could lead to outdoor avoidance and decreased sunlight exposure

Surgical stress response:

Corrective spinal surgery is a major operation with induced series of metabolic, inflammatory, and endocrine changes throughout body. This major trauma stimulates pituitary gland to increase secretion of corticotrophin and growth hormone with consequent increase of cortisol (the stress hormone) from adrenal glands. Cortisol is a catabolic glucocorticoid with major effects on protein breakdown and muscle wasting. Cortisol increases osteoclast activity while reducing the development and differentiation of osteoblasts. It also reduces the production of sex hormones. Cortisol increases renal calcium excretion and concurrently reduces intestinal calcium and vitamin D absorption. It also can cause increased degradation of vitamin D.[18] Cortisol degrades vitamin D binding protein and interferes with its hepatic production.[19] This results in decreased active vitamin D availability to remote tissues.

It has been shown that production of active vitamin D is markedly reduced after elective major surgery.[20] Surgical stress response can cause a profound change in the protein distribution between the intra- and extravascular compartments. This rapid fluid shift may influence vitamin D reabsorption at the renal tubule. Additionally, the tissue requirement of vitamin D is increased during acute stress. The secondary hyperparathyroidism induced by hypocalcemia in acute stress phase may increase vitamin D consumption in tissues, exacerbating vitamin D insufficiency and deficiency.[21]

#### **Postoperative pain:**

Combination of extensive tissue dissection, mechanical irritation, inflammation, and instrumentation could cause severe pain and disability in early postoperative days and the following months of corrective spinal surgery. It is estimated that about 37.8% have chronic pain at 3 months, while 41.8% of patients have persistence of pain a year following surgery.[22] Preoperative pain is a risk factor for postoperative pain and chronic pain. Postoperative pain is associated with disability and reduced patient satisfaction.[23] Postoperative pain may influence adequate dietary intake, mobilization, and outdoor physical activity.

Postoperative pain management in adolescents is challenging. On the other hand, the majority of patients are girls with increased susceptibility to pain.

Morphine is the best established and most widely used analgesia following corrective spinal surgery. However, its use is associated with nausea and vomiting compromising appropriate nutrition. Epidural analgesia is another effective method of analgesia, but it is associated with immobility. Glucocorticoids have both analgesic and anti-inflammatory effects, but they interfere with the synthesis of active vitamin D and its biological action at the tissue levels.[24] Acetaminophen and NSAIDs use are also associated with chronic functional gastrointestinal disorders including dyspepsia, reflux, and mucosal erosions. These disorders could result in decreased vitamin D absorption through in-appetite, reduced mucosal surface area, and inflamed intestinal epithelium.[25]

#### **Postoperative complications:**

The overall complication rate of surgery for AIS is about 1.5%, with the surgical site infection as the most common complication.[26] Antibiotics such as rifampin may interfere with vitamin D through induced catabolism of 1,25dihydroxyvitamin D.[27]

New neurological deficit is the second common complication postoperatively. Immobilization induced by nerve root injury, incomplete or complete spinal cord injury could lead to physical inactivity and associated VDD.

In cases of implant-related complications prolonged hospital stay and repeated surgeries predispose patients to physical and psychological distress. These might result in inadequate dietary intake and reduced outdoor activities.

## Bracing:

Postoperative bracing is still described by some surgeons and is widely advocated in some institutions. However, bracing has its own drawbacks and can significantly affect the quality of life of the AIS patients. Bracing can be psychologically difficult for adolescents and uncomfortable to wear. Bracing could potentially cause over-dressing and outdoor activity avoidance either due to its weight or visual appearance. Adolescents who wear braces have reported wearing additional outerwear or loose-fit clothing styles to maintain a positive body image and minimize the unpleasant feelings caused by the brace.[28] This overdressing habit could result in decreased sun exposure and vitamin D synthesis.

Bracing could also result in chest wall compression, decreased vital capacity, and increased intra-abdominal pressure. These may lead to in-appetite and some eating disorders and consequent nutritional VDD.[29]

## **Conclusion**:

Here we have reviewed the most key risk factors of VDD in the AIS patients following corrective spinal surgery. Preoperative VDD, ICU admission, pain, surgical complications, stress response, medications, and bracing are probably the main risk factors of VDD postoperatively. However, there are probably other risk factors associated with VDD in this high-risk patients which are not discussed in this narrative review. Further studies are needed to identify risk factors of VDD in patients scheduled for surgical correction perioperatively. Fortunately, the major risk factors of VDD are susceptible to intervention. Risk factor modifications is a key component of the management of VDD in AIS patients. This would probably result in better surgical outcomes and and patient satisfaction.

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No patients's consent was needed due to the nature of the manuscript.

#### **Declaration of interests**

☑ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

□ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Journal Prevention